400th CIRM-funded paper clarifies link between gene variant and Alzheimer's

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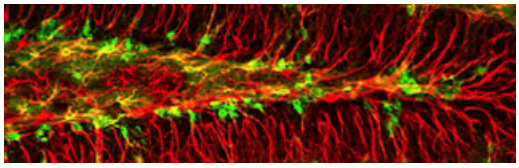
The 400th paper published with CIRM funding also marks the five-year anniversary of the first CIRM board meeting (the actual date was December 17, 2004). The paper, by researchers at the Gladstone Institute and the University of California, San Francisco, illustrates how far the field has come in the five years since the organization's inception, and in the three years since the organization has been funding research.

The paper reveals why people with a particular gene variant called ApoE4 are more likely to develop Alzheimer's disease and identifies possible drug treatments to block the effects of that gene variant. The gene ApoE makes a protein that is involved in lipid metabolism and neuronal repair and remodeling. As with all genes, people can inherit different variants, and each variant makes a slightly different protein.

People with the variant called ApoE4 have long been known to be at higher risk of developing Alzheimer's disease, but nobody has known why. In a press release by the Gladstone Institute, senior author Yadong Huang said:

> "Our findings suggest that apoE4 inhibits the development of newborn neurons by impairing the GABAergic signaling pathway and that boosting this pathway with drugs may be of therapeutic benefit. It might allow us to encourage the development of new neurons from stem cells to replace those lost in apoE4 carriers with AD."



The ApoE4 protein prevents the brain's pool of stem cells from replacing cells lost to Alzheimer's disease. Understanding this basic biology could result in a new drug that blocks the inhibitory effects of ApoE4 and acts as a call to action to the brain's stem cells. (The image shows the brains of mice, with ApoE in green and neural stem cells in red.)

CIRM was voted into existence by 59% of California voters eager for new disease therapies. CIRM has only been funding research for three years due to a lawsuit. In that short time several CIRM grantees have made discoveries about how Alzheimer's develops, how stem cells might be used in a future therapy, and now how drugs might be used to treat the disease in a particular group of people. Each of these is a step toward fulfilling the hope of Calfornians who voted for Proposition 71.

Typical of most CIRM-funded papers, at least one of the authors on the 400th paper is on a training grant. These graduate students, postdocs and clinical fellows working on stem cell projects contributed to 69% of all papers published with CIRM funding. Their work spans the most basic biology â work that is needed in order to understand the basic functionality if stem cells â and projects that are moving those basic discoveries toward the therapies.

The incredible productivity of these grantees is not a surprise. The CIRM Governing Board recognized the importance of pulling students into stem cell projects and funded the first training grants in April 2006 with Bond Anticipation Notes before the agency's legal battles had completed.

Of the 400 published papers, almost a quarter were in high profile publications such as Science, Nature, and the Cell journals.

Cell Stem Cell, December 4, 2009 PMID: 19951691
CIRM funding: Yudong Huang (RN2-00952), Gang Li T2-00003 (T2-00003)

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